REMARKS

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Reconsideration and allowance of the subject application are respectfully requested.

Claims 1-18, 20, 24-34, and 36-47 are pending in the application.

Claims 1 and 27 have been amended to incorporate the subject matter of dependent claim 23. Claim 18 has been amended to be in independent form. No new matter has been added.

The rejection of claims 1-4, 7, 10, 11, 13, 15, 22 and 27 under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent No. 5,858,410 (Muller 410) is obviated by the amendment of claims 1 and 27 to include the subject matter of dependent claim 23. Accordingly, withdrawal of the Section 102 rejection is respectfully requested.

The rejection of claims 1-20 and 22-47 under 35 U.S.C. § 103 as being unpatentable over WO 98/14174 (Desai) in view of Muller is respectfully traversed. The claimed invention is not obvious over Desai in view of Muller for the reasons of record and for the following reasons.

Claims 1-18, 20, 24-34, and 36-45 recite that the process provides a "gentle particle size reduction with minimization of the impairment of the chemical stability of the homogenized material." The background section of the present application at pages 3-4 teaches that a gentle process includes one or more of the following parameters:

- to minimize or exclude contact with water
-to exclude the use of toxicologically undesirable organic solvents such as dichloromethane
-to minimize or avoid the temperature load
-to avoid the addition of toxicologically undesirable additives such as plasticizers
-to minimize or exclude exposure to oxygen
-to avoid melting and to keep the substances to be processed in solid state.

The background section of the present application at pages 4-5 also teaches that cavitation is an implosive and strong force, i.e. not gentle, and that cavitation requires water and higher temperatures to form gaseous water. Thus, the claim language "gentle" requires reduced or without cavitation.

Claims 30, 36, 37, 46 and 47 recite "without cavitation."

Desai teaches away from the claimed invention. See page 18, lines 16-19 of Desai, where Desai describes "[a]cceptable methods of homogenization include processes imparting high shear and cavitation..."

Muller also teaches away from the claimed invention, by teaching that "[t]he dispersing principle is cavitation." See column 5, lines 6-7 of Muller.

Thus, the combination of Desai and Muller clearly teaches to use cavitation as the principle dispersing principle, which is in a direction away from the claimed invention. For this reason alone, the Section 103 rejection should be withdrawn.

The experimental evidence of record rebuts any prima facie case of obviousness based on the combination of Desai and Muller. As discussed previously, Applicants have now found that during high-pressure homgenization using a piston-gap homogenizer, water vapor is created in the form of bubbles, which subsequently implode, otherwise known as cavitation. The resulting implosion shock waves lead to particle diminution. However, many materials are destroyed, melted or otherwise undesirably altered by these violent shock waves (cavitation). See page 3, last paragraph to page 4, first paragraph, in the present translated application.

Applicants have solved these problems by providing a far more gentler method of obtaining the same particle size without using the implosion shock waves (i.e. substantially avoiding cavitation or reducing cavitation):

1) reducing or eleminating the use of water; and/or

2) reducing the temperature of the medium being homogenized.

As discussed above, prior to the present invention, it was believed throughout the art that cavitation was required as the main source of diminution, which belief is supported by Desai and Muller. As a consequence, high pressure homogenization is generally described in water and especially increased effectiveness is claimed

when homogenizing at higher temperatures. The reason for the increased efficiency at higher temperatures is the increased vapour pressure of water at higher temperature which provides increased cavitation. Therefore, the teachings in Desai and Muller is the need to use water at higher temperatures to provide increased cavitation formation from water vapor to thereby provide particle diminution.

Contrary to this teaching, according to the present invention high-pressure homogenization using a piston-gap homogenizer is performed in media other than water (anhydrous) or water reduced (less than 80% wt.), and/or at lower temperatures to reduce or avoid cavitation from water vapor. Surprisingly, it has been found that even without presence (anhydrous) or presence of reduced amounts of water, still a comparable size diminution can be obtained. Thus, it is believed, without being bound to any theory, that effects other than cavitation are responsible for the observed diminution action. Contrary, to the general knowledge in the art represented by Desai and Muller, Applicants have found that cavitation is not the dominating diminution principle in the present invention. This is further supported by performing homogenization at lower temperatures, e.g. at 20° Celcius or below. A surprisingly similar efficiency in diminution is observed, which is contrary to the general beliefs in the art. Furthermore, there is no increase of homogenization cycles required so that effectiveness of the high-pressure homogenization is about the same compared to homogenization in water using primarily cavitation. This enables processing of hydrolysis sensitive drugs. Please see pages 4-6 of the originally filed application, which further describes the unexpected advantages of the claimed invention.

Desai and Muller, alone or in combination, do not disclose the unexpected advantages associated with reducing or avoiding cavitation in a high-pressure homogenzation method using a piston-gap homogenizor. For these reasons alone, the Section 103 rejection should be withdrawn.

Present claims 46 and 47 recite particles of "5.6 μm or less," which are not included in Desai's particle ranges. For this reason alone, the Section 103 rejection of claims 46 and 47 should be withdrawn.

Claim 25 recites carrying out the process with the exclusion of oxygen. None

of the cited references teach or suggest this limitation. For this reason alone, the Section 103 rejection of claim 25 should be withdrawn.

Claim 26 recites degassing the dispersion medium before use. None of the cited references teach or suggest this limitation. For this reason alone, the Section 103 rejection of claim 26 should be withdrawn.

Claim 41 and 42 recite gassing the matrix material and medium with inert gases. None of the cited references teach or suggest this limitation. For this reason alone, the Section 103 rejection of claims 41 and 42 should be withdrawn.

In view of the many differences between the claimed invention and the theoretical combination of Desai and Muller, and the unexpected advantages of the claimed invention, withdrawal of the Section 103 rejection is respectfully requested.

In view of all of the rejections of record having been addressed, Applicants submit that the claimed invention is in condition for allowance and Notice to that effect is respectfully requested.

Respectfully submitted,

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